

بسم الله الرحمن الرحيم





شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم



جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار





بعض الوثائق الأصلية تالفة





بالرسالة صفحات
لم ترد بالأصل





Faculty of Pharmacy

Department of Pharmaceutics and Industrial Pharmacy

Optimization of nano delivery systems of an anticancer drug

A Thesis

Submitted in Partial Fulfillment of the Requirements for the

Master Degree

In Pharmaceutical Sciences

(Pharmaceutics)

By

Shaymaa Aly Ibraheem Abd-Algaleel

Bachelor of Pharmaceutial Sciences, 2013

Faculty of Pharmacy, Ain Shams University

QC Specialist, Department of Pharmaceutics, Egyptian Drug
Authority (EDA)

2021



Optimization of nano delivery systems of an anticancer drug

A Thesis

Submitted in Partial Fulfillment of the Requirements for the

Master Degree

In Pharmaceutical Sciences

(Pharmaceutics)

By

Shaymaa Aly Ibraheem Abd-Algaleel

QC Specialist, Department of Pharmaceutics, Egyptian Drug Authority
(EDA)

Under the Supervision of

Prof. Dr. Rania Mohamed Hathout

Professor and Head of Department of Pharmaceutics and Industrial
Pharmacy, Faculty of Pharmacy, Ain Shams University

Associate Prof. Abdelkader Aly Metwally

Associate Professor of Pharmaceutics and Industrial Pharmacy, Faculty
of Pharmacy, Ain Shams University

Associate Prof. Hend Mohamed Abdel-Bar

Associate Professor of Pharmaceutics and Industrial Pharmacy, Faculty
of Pharmacy, University of Sadat City

2021

Acknowledgment

First, I thank "**Allah**" for granting me the power to accomplish this work.

I would like to express my deepest thanks to **Prof. Dr. Rania Hathout**, Professor of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Ain Shams University, for suggesting the amazing topic of research, her valuable scientific supervision, her valuable work on the molecular docking part and data curation, constructive advice and continuous guidance throughout the work.

My deepest gratitude and appreciation are expressed to **Dr. Abdelkader Metwally**, Associate Professor of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Ain Shams University, for his dedicated support. His work in molecular dynamics part was the basis of the work. His valuable time and big effort are greatly appreciated.

I am also greatly indebted to **Dr. Hend Abdel-Bar**, Associate Professor of Pharmaceutics, Faculty of Pharmacy, University of Sadat City. Her constructive criticism guided me immensely throughout the work and during the revision of the thesis. I also thank her for providing guidance and follow up especially throughout the in vivo part of this study.

I would also like to thank **Dr. Dina Kassem**, lecturer of Biochemistry, Faculty of Pharmacy, Ain Shams University, for her help in the cytotoxicity work of the study. Besides, I would like to thank my dear **colleagues** and all the **workers** at the Egyptian Drug Authority for their help and support during this work.

Finally, my deepest everlasting thanks and appreciation are for my beloved **family** especially my beloved father for their continuous support and encouragement throughout my life.

والحمد لله رب العالمين.....

Shaymaa Aly

List of Content

LIST OF CONTENT.....	I
LIST OF ABBREVIATIONS.....	VII
LIST OF FIGURES.....	XI
LIST OF TABLES.....	XIV
ABSTRACT.....	i
GENERAL INTRODUCTION	1
SCOPE OF WORK	24
CHAPTER I: IN SILICO OPTIMIZATION OF SESAMOL PAYLOAD IN DIFFERENT LIPID AND POLYMERIC CARRIERS USING MOLECULAR DYNAMICS SIMULATION AND DOCKING STUDIES (DRY-LAB STUDIES).....	
INTRODUCTION	26
EXPERIMENTAL.....	32
• PROGRAMS	32
• METHODS	32
1. All-atom molecular dynamics simulation of lipid and polymeric carriers.....	32

1.1. Lipid systems.....	33
1.2. Polymer systems.....	35
2. Preparation of sesamol chemical structure for docking	36
3. Molecular docking of sesamol on the virtually constructed carriers.....	36
3.1. AutoDock Vina.....	37
3.2. MOE.....	37
RESULTS AND DISCUSSIONS.....	39
1. Molecular dynamics simulation results.....	39
2. Molecular docking experiments results.....	40
CONCLUSION.....	45
CHAPTER II: PREPARATION AND CHARECTERIZATION OF SESAMOL-LOADED SLN AND SESAMOL-LOADED PN _s FOR THE VALIDATION OF THE DRY-LAB STUDIES	
INTRODUCTION.....	46
EXPERIMENTAL.....	53
• MATERIALS.....	53
• EQUIPMENT.....	53
• METHODS.....	54

1. Construction of standard calibration curves of sesamol.....	54
2. Determination of sesamol thermal stability.....	54
3. Preparation of different sesamol-loaded nanoparticles.....	55
3.1. Preparation of sesamol-loaded SLN.....	55
3.2. Preparation of sesamol-loaded PNs.....	56
4. Characterization of sesamol-loaded SLN and sesamol-loaded PNs.....	56
4.1. Measuring PS and PDI.....	56
4.2. Measuring drug content%, EE% and drug payload.....	56
4.3. Morphology of the SLN and PNs optimized formulations using TEM	57
5. <i>In vitro</i> release experiments	58
6. Statistical analysis.....	58
RESULTS AND DISCUSSIONS.....	60
1. The standard calibration curves of sesamol in methanol and PBS pH 7.4.....	60
2. Results of the sesamol thermal stability study and the effect of tween 80 addition.....	60
3. Characterization of sesamol-loaded SLN and sesamol-loaded PNs.....	62

3.1. PS and PDI measurements	62
3.2. Drug content%, EE% and drug payload measurements	63
3.3. Comparison of wet-lab vs dry-lab studies and selection of optimum formulations.....	65
3.4. Morphology of the SLN and PNs optimized formulations using TEM	68
4. <i>In vitro</i> release experiments	69
CONCLUSION	72
CHAPTER III: CYTOTOXICITY ASSAY AND IN VIVO STUDIES OF THE SESAMOL-LOADED SLN AND SESAMOL-LOADED PNs OPTIMIZED FORMULATIONS.....	
INTRODUCTION	74
EXPERIMENTAL.....	82
• MATERIALS.....	82
• EQUIPMENT	82
• ANIMALS.....	82
• METHODS	83
1. Cytotoxicity studies.....	83
1.1. GL261 cell line culture and maintenance.....	83
1.2. Cytotoxicity evaluation using MTT assay.....	83
2. <i>In vivo</i> pharmacokinetics studies.....	84
